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New Onset Psychosis Associated with Asymptomatic COVID-19 Infection: A Case Report and Possible Mechanisms

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Abstract

The COVID-19 virus is classically associated with acute respiratory tract infectious syndrome. However, specific symptoms are known to persist following viral resolution, including psychiatric symptoms. Our case report outlines a 42-year-old male patient who was incidentally found to have an asymptomatic COVID-19 infection during the initial workup for unexplained paranoia and delusions. All other organic or substance-induced causes were ruled out, raising suspicion for COVID-related psychosis. His psychotic symptoms were treated with risperidone but continued for months after his discharge from the hospital. This case highlights the potential for psychiatric manifestations connected to the COVID-19 virus and adds to the body of literature that suggests a correlation between viral infection and progression to a psychiatric illness.

Keywords: COVID-19; Psychosis; Long COVID; Neuropsychiatry; Consult psychiatry; Paranoia.

Introduction

COVID-19 is an RNA virus, SARS-CoV-2, that predominantly causes a respiratory tract infection. Four identified syndrome stages exist, although some individuals will remain asymptomatic or only develop mild symptoms. Fever, myalgias, cough, and other typical upper respiratory infection manifestations characterize the first stage. The second stage involves increasing dyspnea and pneumonia, which worsens to vasculopathy due to cytokine storm in the third stage. Either recovery or deterioration into death forms the fourth stage [1]. Many survivors of COVID-19 report various persistent symptoms, such as anosmia; however, psychiatric symptoms are less identified and studied. Our case describes a previously healthy male patient who developed psychotic symptoms in the context of asymptomatic COVID-19 infection, which remained following viral resolution.

Case presentation

A 42-year-old Hispanic divorced male with no psychiatric history, substance abuse, or history of violence was brought to the hospital by family members who had concerns about recent paranoia and violent behavior. Incidentally, he was found to be COVID-19 positive on routine screening and thus was admitted to medicine. Psychiatry was consulted for assistance after an involuntary psychiatric hold was placed in the Emergency Department.

The patient's psychiatric history was obtained from the patient and his sister as his paranoia and delusional state made him an unreliable historian. The patient had no prior psychiatric history, normal childhood development, good social skills, and no history of depression, anxiety, social isolation, paranoia, impulsivity, bizarre thoughts or behaviors, suicidal ideation or

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attempts, or violence. He joined the military when he was 19 years old and worked in the military police. He had no children and was divorced; he reports that he was married when he was younger and divorced due to different life goals (wanting children and moving to the United States) rather than personal conflicts. Both the patient and sister confirmed that the patient never used recreational substances, and a urine drug screen confirmed this on admission. The patient had always been able to hold a stable job and pay his bills, and he had never been undomiciled.

The patient was alert, pleasant, cooperative, and oriented x4 on mental status examination. He described his mood as "fine" and his affect as euthymic, but he became distressed when describing his recent history. His thoughts were circumstantial. His thought content was remarkable for prominent delusions, both paranoid and grandiose in nature. He denied suicidal or homicidal ideation. He denied auditory-visual hallucinations, but he did report seeing energies around people. There were no noted deficits in memory, attention, or language. Insight and judgement were poor as the patient was denying his COVID-19 positive testing and the presence of psychiatric symptoms.

His sister reports that she noticed a significant change in his cognition and personality prior to admission compared to his previous behavior. Prior to admission, the patient's family was concerned as the patient was possibly facing eviction from his apartment. When asked about the events that lead to this possible eviction and ultimately him coming to the hospital, the patient claimed that "fake police" forcibly removed him from his apartment following an altercation with a neighbor, the patient in fact reported biting a police officer because "he wasn't a real cop." His delusions revolved around being a secret investigator into unlawful "fake jails" and that previously he was illegally detained and "beaten and raped in the fake jails," and that he couldn't tell his family in order "to keep them safe". He went on to say he was looking into "gems and chemicals in the water system." The patient was calm and cooperative with staff but refused all medications as he felt "my body will heal itself" and was distrustful of "chemicals." He frequently used "fire breathing," also known as 'ujjayi' breathing, a yoga technique that involves controlling your breath with your diaphragm, to heal himself. He also frequently penned disorganized, illogical letters and drawings, referring to them as "sacred writings," which he believed clarified the workings of the world and aided him in his investigations. He reports that he wanted to stop working his job to dedicate time to his investigation. He slept roughly six hours, felt well-rested, and reported a good appetite.

As this was the first time the patient had experienced psychosis per the patient's family and military/veteran's records, a full diagnostic workup was completed. Initial laboratory testing on admission, the patient had increased inflammatory markers (WBC, ANC, LDH, D-Dimer) and two positive COVID-19 tests. He denied ever having symptoms of COVID-19, including respiratory symptoms, fever, chills, loss of taste or smell, fatigue, muscle aches, headaches, nausea/vomiting, or diarrhea. The patient had intermittent hypertension during his 19-day hospitalization but refused blood pressure medications. No other pre-existing medical conditions or other medical conditions were found on medical workup. Confounding contributors to psychiatric symptoms were ruled out with a negative anti-treponema pallidum IgG, nonreactive HIV antigen-antibody, normal TSH, B12, and folate. Of note, his vitamin D was low at 5 ng/mL. CT Head without contrast showed no acute intracranial process, and MRI brain with and without contrast showed no significant intracranial abnormalities. EEG showed normal routine awake and asleep patterns with no evidence supporting a seizure diagnosis. See Table 1 for full details of medical workup.

The patient was kept on the medicine floor for ten days for clearance of COVID-19 infection under an involuntary psychiatric hold and was cleared for psychiatric admission. The patient was receiving Risperidone 1 mg PO BID with a slight improvement in symptoms before being transferred to the inpatient unit. Once inpatient, his Risperdal was up titrated to 3 mg BID. Weeks later, the patient was discharged with follow-up in a mental health outpatient clinic. He was able to secure stable housing prior to discharge.

Table 1: Medical workup.

Parameter	Value on admission	Normal range
Hematologic counts		
WBC	$10.12x10^9$/L	$3.9\text{-}9.9x10^9$/L
ANC	$6.81x10^9$/L	$1.73\text{-}6.37x10^9$/L
Hemoglobin	14 g/dL	13-17 g/dL
Electrolytes		
Sodium	140 mmol/L	136-145 mmol/L
Potassium	2.9 mmol/L	3.5-5.2 mmol/L
Inflammatory markers		
Lactate dehydrogenase (LD)	431 U/L	133-226 U/L
C-reactive protein	0.7 mg/dL	0-1 mg/dL
Ferritin	234.7 ng/mL	15-274 ng/mL
D-Dimer	740 ng/mL FEU	0-500 ng/mL FEU
Fibrinogen	395 mg/dL	184-485 mg/dL
aPTT	35 sec	25.1-36.5 sec
Psychiatric screening		
Anti-treponemal pallidum IgG	negative	
HIV antigen-antibody	nonreactive	
TSH	2.17 µIU/mL	0.46-4.7 µIU/mL
Vitamin panel		
Vitamin D	5 ng/mL	10-30 ng/mL
Vitamin B12	692 pg/mL	218-1124 pg/mL
Folate	5.9 ng/mL	>5.4 ng/mL
Substance screening		
Urine drug screen	negative	
Salicylate	<5.0 mg/dL	15-30 mg/dL
Acetaminophen	<1 mcg/mL	10-30 mcg/mL
Infectious markers		
Blood culture	No growth	
Sars-Cov-2 IgG Index	7.28 Index(S/C)	0-1.39 Index(S/C)
COVID- 19 Diagnostic	Detected	

Discussion

Since the emergence of SARS-CoV-2, literature continues to grow on the sequelae of post-COVID-19 infection, providing significant findings in every organ system [2]. While the focus of research has understandably been placed on the pulmonary and cardiovascular systems, a growing body of literature is dedicated to the effects on the brain.

Acute neuropsychiatric manifestations of COVID-19 infection include confusion and alteration of consciousness, after which many survivors experience objective cognitive deficits, colloquially known as "brain fog" [3]. In addition, the many lifestyle changes necessitated by the pandemic, most importantly self-isolation, have been linked to common neuropsychiatric symptoms such as anxiety and depression [4]. Although there is currently no consensus on the risk factors for psychiatric sequelae from COVID-19 infection, many studies have identified some associations for depression, anxiety, and Post-Traumatic Stress Disorder (PTSD). This case study adds to the growing literature of COVID-19 associated psychosis as it differs from what are currently identified risk factors – namely female sex, history of psychiatric diagnosis and treatment, prolonged and/or severe COVID symptoms, or recent loss of a loved one [5,6]. Additionally, many studies found that these risk factors led to predominantly mood disorders, such as anxiety, depression, and PTSD.

More alarming cases of psychosis, hallucinations, and otherwise disorganized behavior have also been reported during both acute and chronic phases of infection [7]. A landmark retrospective review of more than 230,000 patients found a significantly higher risk of psychotic disorders in the 6-month follow-up period of patients after COVID-19; 1.4% of patients showed psychotic disorders, with 0.42% as first psychotic episodes [8]. The rates from COVID-19 were statistically significantly higher than the rates of psychosis from influenza and other respiratory infections, further highlighting the importance of continued psychiatric research on COVID-19.

While it is premature to conclude that COVID-19 infection has a causative role in psychotic disorders, SARS-CoV-2 has been shown to cross the blood-brain barrier via immune-mediated damage and thromboembolism [4,5,7,9]. Brain tissue from autopsies of patients with nucleic acid-proven COVID-19 infection supported blood-brain barrier involvement as megakaryocytes, large cells that produce platelets, were found in brain cortical capillaries. Megakaryocytes are not found in the brain or their vessels, and this is the first recorded finding where the breakdown of the blood-brain barrier allowed their passage [10]. There has also been evidence suggesting SARS-CoV-2 might infect endothelial cells of the brain. It has been posited that dysfunction to the blood-brain barrier could occur during the body's response to infection or through other direct interactions of the virus and its components with the blood-brain barrier [11]. By now, it is well-known that COVID-19 infection causes high rates of thrombotic-related complications [12]. Lesser known is that these coagulation abnormalities include cerebral microemboli and immune-activated complement-mediated Thrombotic Microangiopathy (TMA). Neuroimaging of COVID-19 patients with abnormal mental status and evidence of upregulated coagulation factors showed evidence of TMA [11]. These findings on clotting and thrombosis further support blood-brain barrier disruption as the likely pathophysiology of the neuropsychiatric sequelae of COVID-19 infection.

Another proposed mechanism for COVID-19 mediated psychiatric symptoms looks at a different mechanism of increased CNS inflammation and immune mechanisms. Both central and peripheral mast cells are overstimulated during COVID-19 infection, an increased mast cell activation is associated with an increase in psychiatric symptoms and illnesses, including paranoid psychosis and hallucinations [13]. Whether initiating from peripheral or central mast cells, mediators can be transported by the bloodstream to the brain where their effects are integrated with mast cell-mediator-related changes in neural afferents from the periphery. The resulting changes in neuronal reactions can clinically manifest as psychiatric symptoms, this is classically seen in Mast Cell Activation Disease which is also mediated by this mechanism of action and has significant psychiatric co-morbidities associated [14].

This case report adds a new layer of complexity to the growing case of psychiatric sequelae surrounding COVID-19 infection, as current case reports identify resolution of symptoms following improvement and resolution of COVID-19 infection. Our patient's continued paranoid and bizarre delusions persisting outside of his acute infective phase without any respiratory symptoms or prior psychiatric history. This presentation is a novel finding that may signal that "long COVID" sequelae may have more far-reaching impact that previously presumed.

Conclusion

This case followed the progression of psychotic symptoms in a patient with an asymptomatic COVID-19 infection. It is particularly novel in that our patient was male with no pre-existing psychiatric conditions and that his psychiatric symptoms persisted despite resolution of acute infection. While "long COVID" is typically associated with various physical manifestations, it is essential to be cognizant of the potential for psychiatric sequelae. As research has shown multiple possible mechanisms COVID-19 has that effect acute and chronic inflammation in the brain, changes in neuronal action, and disruption of the blood-brain barrier there may be several neuropsychiatric sequelae that can have significant impact on psychiatric screening and practice in the future.

Declarations

Conflict of interest: The authors declare that the research was conducted without any commercial or financial relationships that could be identified as a potential conflict of interest.

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